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I am Me: Brain systems integrate and segregate to establish a multidimensional sense of self

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ABSTRACT

Humans experience a sense of self, which is proposed to emerge from the integration of intrinsic and extrinsic self-processing through the propagation of information across brain systems. Using a novel functional magnetic resonance imaging (fMRI) paradigm, we tested this hypothesis in a non-clinical sample by modulating the intrinsic and extrinsic self-relatedness of auditory action consequences in terms of identity and agency, respectively. In addition, the relevance of individual traits associated with altered self-experiences (e.g., psychosis-like experiences) was examined. The task-evoked fMRI results showed distinctive associations between the neural coding of identity and negative affect traits, and between agency and psychosis-like experiences. Most importantly, regarding the functional connectivity analysis, graph theoretical measures demonstrated that the simultaneous processing of identity and agency relies on the functional integration and segregation of default mode, sensorimotor, language, and executive brain networks. Finally, cross-network interactions mediated by executive and sensorimotor regions were negatively associated with psychosis-like experiences when the intrinsic and extrinsic self-relatedness of action consequences conflicted. These findings provide evidence that the self is a multidimensional phenomenon rooted in the functional interactions between large-scale neuronal networks. Such interactions may have particular relevance for self-experience alterations.

1. Introduction

How does the sense of self emerge from our perceptual interactions with the world? In research from the past decades, the self has been increasingly portrayed from multiple perspectives that differentiate between its intrinsic and extrinsic components (Christoff et al., 2011; Van den Bos and Jeannerod, 2002). Intrinsic self-processing concerns the perception of information as belonging to oneself or as personally relevant and can be indicated by the term “identity” (Northoff, 2011; Apps and Tsakiris, 2014; Heydrich et al., 2018). It depends on the integration of information from memory, personal narrative, and interoception (Damasio, 1998; Gallagher, 2000; Northoff and Panksepp, 2008). In contrast, extrinsic self-processing regards the experience of oneself as the source of one’s own actions and their consequences (Haggard, 2005; Gallese and Sinigaglia, 2010) through the comparison of action predictions and intentions with action feedbacks (Moore, 2016; Haggard, 2017), and can be designated “agency”. Extrinsic and intrinsic self-processing represent two essential dimensions of the sense of self.

However, the unification of these perspectives and their clinical potential remains to be further developed and clarified (Ebisch and Aleman, 2016).

We propose that, during voluntary actions with sensory consequences, these components are naturally unified in a bidirectional process. Intrinsic self-processing is internally directed by referring sensory input to an inner self (Rogers et al., 1977) and is supported by both sensory networks (Heydrich et al., 2018; Gallese and Sinigaglia, 2010) and default networks (Northoff and Panksepp, 2008; Andrews-Hanna et al., 2014). By contrast, extrinsic self-processing is externally directed due to its intentional nature (Prinz, 2012) and is supported by executive/attentional and sensorimotor networks (Chambon et al., 2013; Van Kemenade et al., 2019) that encompass fronto-parietal regions including the precuneus, dorsolateral prefrontal cortex, insula, and temporo-parietal junction (Sperduti et al., 2011; Maurer et al., 2016) as well as the cerebellum (Darby et al., 2018; Sokolov et al., 2017).

A common example of multidimensional self-relatedness regards language production: when speaking, I can recognize my own verbal expressions (Levelt, 1983) since I recognize the words that I intentionally

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chose to communicate (extrinsic self: agency) and that are being pronounced in my own voice (intrinsic self: identity). However, these two aspects have only been investigated separately in previous studies (Fu et al., 2005; Zheng et al., 2011; Reznik et al., 2014; Chai et al., 2016). Disrupted interactions between intrinsic and extrinsic self-networks could be particularly relevant for self-disturbances in psychosis (Ebisch and Aleman, 2016) as shown by an aberrant coupling between language and auditory processes in auditory hallucinations concurrent with disrupted self-recognition (Ćurčić-Blake et al., 2017).

With the present study, we investigate how the self emerges from the interaction between intrinsic and extrinsic self-related processing of action consequences. In this regard, we focus on the segregation and integration of functional brain networks (Sporns, 2013). Segregation indicates the presence of identifiable communities (i.e., modules) within the network that are possibly carrying out distinct cognitive operations with limited information exchange (Sternberg, 2011). Integration refers to an increased association between modules, possibly mediated by functional hubs (Tomasi and Volkow, 2011) that imply a reduced number of necessary modules and possibly contributes to increased information exchange (Godwin et al., 2015). In addition to segregation and integration, we also investigated the relationships between brain measures and clinically relevant psychological traits that are likely to involve interactions between extrinsic and intrinsic processing.

We report a functional magnetic resonance imaging (fMRI) experiment developed to elucidate the interactions between the extrinsic (agency) and intrinsic (identity) self-relatedness of auditory (verbal) action consequences. Thirty-nine healthy adult participants were asked to choose among carefully controlled, visually presented syllables to form meaningful words during fMRI scanning. Auditory feedback consisted of words that were either selected by the participants or not to create a context of self-agency (SA), in which participants always heard the chosen word throughout the run, and a context of other-agency (OA) in

which participants heard a pseudo-randomly chosen word in each trial. Thus, this distinction pertains to extrinsic self-processing. Additionally, auditory stimuli were presented either in the voice of the participant or in a stranger's voice to create contexts of self-identity (SI) and other-identity (OI). Hence, this experimental manipulation pertains to intrinsic self-processing. An example trial is illustrated in Fig. 1. All participants also underwent a series of self-report measures of psychosis-relevant traits.

First, we analyzed stimulus-evoked brain activity to untangle brain networks involved in agency and identity processing. By specifically linking language and auditory systems to self-related processing, we expected an association of agency with frontal and temporal language regions supporting word content processing (Chai et al., 2016), and of identity with temporal auditory regions involved in voice recognition (Fu et al., 2005). Furthermore, given the extrinsic self-disturbance structure of psychotic symptoms (Nelson et al., 2008; Haggard, 2017), we predicted that agency would be linked with psychosis-like experiences. By contrast, since intrinsic self-impairments have been described mainly in relation to emotional disturbances (Van der Meer et al., 2010; Hasler and Northoff, 2011), voice identity was expected to be associated with affective traits in affect-related brain networks (e.g., insula, prefrontal cortex, cingulate cortex).

Secondly, brain functional connectivity was examined to elucidate how agency and identity are entangled in the brain. Previous studies showed the relevance of the modular organization of the brain (Bullmore and Sporns, 2009) for the conscious awareness of external stimuli through global information integration across networks (Godwin et al., 2015). We hypothesized that the modular organization of the brain would rearrange when shifting between self-relatedness and other-relatedness of external stimuli. In particular, brain networks may functionally reorganize depending on the processing of intrinsic (default mode and sensory networks) or extrinsic (sensorimotor, executive and

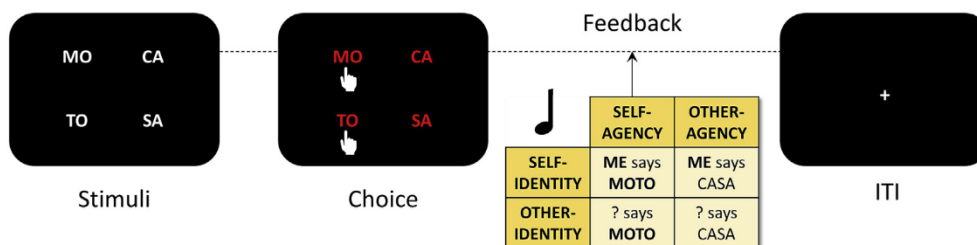


Fig. 1. Experimental paradigm: example trial. Stimuli (syllables) were presented for 4–5 s. During the stimuli presentation, participants were instructed to detect the two meaningful Italian words (in this case: “MO-TO” and “CA-SA”). After this period, the letters turned red and the participant selected one syllable from the upper row and one syllable from the lower row to form one of the two meaningful words. The index finger was used to select the left syllable, and the middle finger was used to select the right syllable between each couple (the pointing hands in the figure are indicating the example choice made in this trial but were not shown during fMRI). Immediately after the word selection, participants received an auditory feedback consisting of a voice pronouncing a word and a white fixation cross appeared for 6–10 s (intertrial interval, ITI). In two fMRI runs, the auditory feedback was always the word chosen by the participant (self-agency runs, SA), while in the other two runs auditory feedback could be in pseudorandomized order either the word selected by the participant (50% of the trials) or the other word (other-agency runs, OA). Moreover, in two runs the word was presented in the voice of the participant (self-identity runs, SI), while in the other two runs it was presented in a sex-matched stranger's voice (other-identity runs, OI).

language networks) self-relatedness of verbal auditory action consequences. An increased network integration may reflect an efficient assimilation of self-related information. By contrast, the absence of self-relatedness may be associated with increased segregation of the same brain networks. Finally, higher scores in psychosis-related traits were hypothesized to be linked with decreased interactions between self-related brain systems (in particular regarding sensorimotor, default mode, language, and fronto-parietal networks), possibly hindering the exchange of intrinsic and extrinsic self-information at the basis of a coherent sense of self (Ebisch and Aleman, 2016; Ćurčić-Blake et al., 2017).

2. Materials and methods

2.1. Participants

Thirty-nine healthy Italian adults (19 females and 20 males aged 23 ± 2) without a history of psychiatric or neurological disease and without contraindications for MRI scanning participated in the fMRI experiment. For the factor analysis on the psychometric measurements, an additional sample of 62 participants without a history of psychiatric or neurological disease was included (participants in another, independent experiment that is not reported here; see Di Plinio et al., 2019) to obtain a cohort of 101 participants that completed the same series of psychological questionnaires (total cohort: Italian healthy adults; 47 males and 54 females aged 24 ± 3). Participants had the same primary and secondary education, and a variable number of college years (4 ± 3) depending on their age. All participants had a normal or corrected-to-normal vision and provided written informed consent before taking part in the study. The experiment was approved by the local ethics committee.

2.2. Psychometric scales and factor analysis

Associations between brain physiological variables (evoked activity, network metrics) and psychosis-relevant personality traits were investigated. Considering the relationship of the sense of agency and of schizophrenia with schizotypal traits and psychosis-like experiences (Vollema et al., 2002; Asai et al., 2008; Van Os et al., 2009), tolerance of uncertainty (Jeannerod, 2009; Moore and Fletcher, 2012; Valdesolo and Graham, 2014), and anxiety (Achim et al., 2009; Gallagher and Trigg, 2016), we administered the following questionnaires in addition to general personality traits (Ross et al., 2002; Asai et al., 2011) measured by the Big Five Questionnaire (Soto and John, 2017) (BFQ): the Intolerance of Uncertainty Scale (Carleton et al., 2007) (IUS-12), the Schizotypal Personality Questionnaire (Raine, 1991) (SPQ), the Community Assessment of Psychic Experience (Konings et al., 2006) (CAPE), the State-Trait Anxiety Inventory (Spielberger et al., 1983) (STAI2). Further details about the questionnaires are provided in the Supplementary File.

As also described in a previous study (Di Plinio et al., 2019), the scores from the 101 participants on the subscales of these questionnaires were used as input for a factor analysis with orthomax rotation to obtain orthogonal trait factors. Prior to the factor analysis, a parallel analysis (PA) (Horn, 1965; Ledesma and Valero-Mora, 2007) was employed to select the number of factors to use in the factor analysis. PA uses a Monte Carlo statistical procedure to generate null distributions of simulated eigenvalues starting from random datasets (10,000) with the same sample size and the same number of variables as the original dataset. Then, the eigenvalues from the original factor analysis were compared with those generated using PA. The number of factors to retain for the factor analysis was selected as the number of eigenvalues above the 95th percentile from the null distribution. Anderson-Darling tests (Anderson and Darling, 1954) were used to assess the normality of the 5 psychometric factors.

To show the appropriateness of the factor analysis in our study, we used a Monte Carlo measurement of the Tucker's congruence coefficient (Korth and Tucker, 1976; Lorenzo-Seva & ten Berge, 2006; de Winter

et al., 2009). The original sample ($N_{\text{tot}} = 101$) was randomly divided into two subsamples (N_1, N_2) and the factor analysis was run independently on the two samples. This procedure was repeated 1000 times with different sample sizes ($N_1 = N_2 = [20, 25, 30, 35, 40, 45, 50]$). At each cycle, we estimated Tucker's congruence coefficient (K) between factors obtained from N_1 and those obtained from N_2 . Values of K were averaged within each sample size and a hyperbolic trend was fitted to estimate the predicted K relative to our sample size (N_{tot}).

2.3. fMRI data acquisition and preprocessing

Functional images were acquired using a Philips Achieva 3T scanner installed at the Institute for Advanced Biomedical Technologies (Gabriele D'Annunzio University, Chieti-Pescara, Italy). Whole-brain functional images were acquired with a gradient echo-planar sequence using the following parameters: repetition time (TR) = 1.2 s, echo time (TE) = 30 ms, field of view = $240 \times 240 \times 142.5$ mm, flip angle = 65° , voxel size = 2.5 mm^3 , slice thickness = 2.5 mm. A high-resolution T1-weighted whole-brain image was also acquired after functional sessions using the following parameters: TR = 8 ms, TE = 3.7, FoV = $256 \times 256 \times 180$ mm, flip angle = 8° , in-plane voxel size = 1 mm^3 , slice thickness = 1 mm. Each participant performed four fMRI runs that consisted of 376 vol each. Each run lasted approximately 7.5 min and included thirty-two experimental trials as described below.

The preprocessing steps and analysis of functional images were implemented in AFNI (Cox, 1996). A slice-timing correction was applied to remove differences in acquisition times between slices. Functional images were deobliqued, despiked, corrected for time-shifted acquisition, and motion-corrected using a six-parameter rigid body realignment before being aligned to the Montreal Neurological Institute (MNI) standard brain using non-linear warping. During the preprocessing steps, the motion parameters for each participant were collected to be used in the deconvolution step. The functional images were scaled to have voxels with a mean value of 100. A Gaussian filter of 5 mm full-width at half-maximum was applied to spatially smooth the functional images.

In addition to these steps, the participants' residual time series obtained after single subject GLMs were censored (volumes with 10% or more outliers across voxels and volumes with Euclidean norm of the motion derivative exceeding 0.3 mm were excluded) and band-pass filtered (interval: 0.01–0.10 Hz) in a single regression step (Caballero-Gaudes and Reynolds, 2017) for the functional connectivity analysis.

2.4. Experimental procedure and stimuli

Stimulus timing and delivery were controlled using E-Prime software (Schneider et al., 2012). Behavioral responses were recorded using a Cedrus Lumina pad system interfaced with the stimulus presentation PC. In each trial, the participant was presented with four white syllables forming a square on a black screen placed behind the MRI scanner. The participants watched the screen through a mirror placed above their eyes. The two upper syllables could be combined with the two lower syllables to form two different Italian bi-syllabic words and two bi-syllabic non-words (see the Supplementary File for word characteristics and selection procedures). The participant was instructed before each fMRI run to spot both words and then to choose one of them. When the syllable color turned red, the participant had to select one syllable from the upper two (first button press) and one from the lower two (second button press) to form the selected word. Button presses were performed using the index (left syllable) and middle (right syllable) fingers of the right hand. Trials in which the behavioral response occurred after the response phase (during the inter-trial) and trials in which the participant used the syllables to form non-meaningful words were considered errors. Behavioral scores are reported in the Supplementary File and did not differ across the conditions (Fig. S1).

After the word selection, participants received an auditory feedback consisting of a voice pronouncing a word (see Supplementary file for

sound recording procedures). The participant was instructed to listen to the word and to evaluate whether the voice was his/her own and whether the word was the one she/he selected. This feedback was presented immediately after the selection of the second syllable. Of note, we do not use the term ‘feedback’ to denote information given back to the participant regarding her/his performance. Instead, the feedback regards an auditory stimulus that returns to the participant after the syllable selection and that is presented in relation to the participant’s choice.

The auditory feedback defined the agency and identity factors of the experiment. A factorial design was used with two within-subject factors, each with two levels: identity (self, SI; other, OI) and agency (self, SA; other, OA). In two fMRI runs, the auditory feedback was always the word chosen by the participant to create a self-agency context (SA runs), while in the other two runs auditory feedback could be, in pseudorandomized order, either the word selected by the participant (50% of the trials) or the alternative word to create an other-agency context (OA runs). Moreover, in two runs the word was presented in the voice of the participant (SI runs), while in the other two runs it was presented in a sex-matched stranger’s voice (OI runs). Thus, each run could be attributed to one of four conditions: 1) SI-SA, 2) SI-OA, 3) OI-SA, 4) OI-OA. The position of the syllables was controlled so that in half of the trials the meaningful words were formed using syllables at the same side of the screen (left-left or right-right) while in the remaining half the words were formed using syllables at opposite sides of the screen (left-right or right-left).

Concerning the auditory feedback, in addition to the instructions above, the participants were also explained before the fMRI runs that the voice could be their own voice or someone else’s voice and that the presented words could be those selected by themselves or by someone else. After the fMRI runs, all the participants included in the fMRI study were asked if they recognized their own voice vs. other’s voices as well as contexts of agency vs. non-agency after performing the task. All participants were able to correctly state in which run they heard their own voice and in which run they consistently heard the word they selected.

The order of the runs was counterbalanced across the participants. It could be argued that having four different conditions in four different runs could cause predictability/order effects or potential changes in the baseline. However, since the participants were not told that there were four different conditions, it is unlikely that the order of the different runs produced undesired predictability effects. Concerning the baseline, in AFNI GLMs this is defined as the null hypothesis of the model, thus including the mean level of the signal, slow drifts, motion parameters, and both cerebrospinal and white matter signals. This unbiased baseline avoids the introduction of false deactivations, or relative deactivations, which can appear after subtracting a control condition (e.g. fixation) from the condition of interest, or after modeling the baseline as the mere average activity of the voxel in a certain time interval.

2.5. Task-evoked activity analysis

Brain activity was estimated using a finite impulse response model in AFNI after the preprocessing pipeline. The hemodynamic shape was modeled from 1.1 to 11.0 s after the stimulus onset using ten basis functions covering the entire trial. A generalized linear model (GLM) was used at the single-subject level. Error trials, if existed, were modeled separately. Only correct trials were considered in this study. Motion parameters obtained during preprocessing, white matter signal, cerebrospinal fluid signal, and polynomial drifts were used as additional nuisance regressors.

Group analysis on task-evoked activity was performed using a mixed-effects model (Chen et al., 2015) in which identity and agency were treated as fixed effects and a random intercept was added at the subject level. Statistical results were corrected for multiple comparisons using cluster correction (Cox et al., 2017) (voxel-wise $p < .001$, cluster size > 35 voxels; threshold $\alpha < 0.05$). To investigate both fixed effects and interactions, all runs of all participants were included in the analyses:

we refer to an effect of the fixed term *identity* when a significant difference was found between self-identity runs (SI-SA; SI-OA) and other-identity runs (OI-SA; OI-OA); we refer to an effect of the fixed term *agency* when a significant difference was found between self-agency runs (SI-SA; OI-SA) and other-agency runs (SI-OA; OI-OA); we refer to an *interaction* effect when a difference in agency or identity was found only for a particular level of identity or agency (e.g. SI-SA $>$ SI-OA). Control analyses to check for the effect of trial type (i.e., match, non-match) within OA trials highlighted no significant differences within regions modulated by the task and are reported in the Supplementary File.

It is unlikely that large significant clusters would entail a single functional brain unit. A large cluster could consist of multiple confining brain units, thus containing multiple peak voxels. To define functional units modulated by each specific level of the analysis (agency, identity, interaction), we used an automated search of local maxima using the function 3dExtrema within the t-statistic maps. In other words, this procedure was used to break down the clusters in subparts (regions of interest, ROIs) for a more precise definition/presentation of the results (see the Supplementary File for details).

2.6. Effect of psychometric scales on brain activity

The effects of the five psychometric factors on task-induced brain activity were estimated in each ROI using mixed models in which the five psychometric factors were used as continuous predictors. The dependent variable consisted of the activity estimated in each of the ten time points in each condition. Random intercept and slopes were added using *time point* as a grouping variable. The factors were corrected through the box-Cox transformation prior to the regression to improve normality. Only models that (i) were significant after correction for multiple comparisons using Bonferroni-Holm correction, (ii) didn’t show violations of model assumptions, and (iii) showed significant effects after outlier removal were considered significant (see Supplementary File for a detailed description of these control analyses). Since we used the orthomax rotation to obtain orthogonal trait factors, the multiple regression does not entail collinearity issues.

2.7. Functional connectivity

Seed-based functional connectivity (FC) analyses were performed to obtain further information about the broader functional networks involved in agency and identity coding. Average seed-based voxel-wise FC maps were calculated separately for ROIs modulated by identity and agency. Residual FC was calculated using the z-Fisher transform of the Pearson correlation. The resulting FC maps were thresholded (10% strongest connections were maintained) and compared with predefined networks (Di Plinio and Ebisch, 2018). We chose to use these networks because we are investigating task-related features of brain systems and this is the only functional architecture that was derived from both task-evoked activity and resting-state FC.

2.8. Graph analysis

For the graph analysis, whole-brain FC was calculated for a total of 418 nodes using cortical (346 parcels) and subcortical (40 grey nuclei) atlases from Joliot and colleagues (Joliot et al., 2015) plus the cerebellar (32 nodes) atlas from Diedrichsen and colleagues (Diedrichsen et al., 2009). These atlases were chosen because of the integrative method used to define both cortical and subcortical parcels without lateralization biases. The average time series were calculated in each cortical, subcortical, and cerebellar parcel. Matrices of functional connectivity were obtained by calculating the z-Fisher transformed Pearson correlation among time series. Graph analyses were performed using the Brain Connectivity Toolbox (Rubinov and Sporns, 2010) implemented in MatLab. Brain modules were visualized using the software BrainNet Viewer (<https://www.nitrc.org/projects/bnv/>) implemented in MatLab.

Formal definitions of metrics used in graph analysis are reported in Table SIII.

Binary brain graphs were constructed from whole-brain connectivity matrices including the top 10% among the positive connections (Van Wijk et al., 2010; Bassett et al., 2011). Modules were detected using modularity maximization (Porter et al., 2009) through the application of the Louvain algorithm (Blondel et al., 2008; Lancichinetti and Fortunato, 2009). Group-level modular partitions were obtained using community detection algorithms (Lancichinetti and Fortunato, 2012). In line with recent methodological protocols (Betzel et al., 2016), multiple structural resolution parameters (γ) were investigated and the most appropriate ones were selected as those maximizing the adjusted Rand coefficient (Traud et al., 2011). Significant modules were detected applying the Newman-Girvan procedure (Newman and Girvan, 2004) with a threshold of $p < .001$. The percentage of each network (Di Plinio and Ebisch, 2018) covered by each module was estimated to characterize the functional fingerprints of the modules in each condition. Further details regarding the graph analysis are provided in the Supplementary File.

Global statistics of modularity and nodal statistics of participation (Guimerà and Nunes Ameal, 2005) were extracted and analyzed using mixed-effect models to uncover associations between network measures and the five psychometric scales. A two-step procedure was adopted to analyze participation coefficients to exclude statistical biases: in the first step, all the network nodes were included as random grouping variables and the psychometric factors were included as continuous regressors; in the second step, the analyses were repeated after removing nodes with inhomogeneous residuals. To detect context-specific and module-specific interactions, a separate model was used for each condition and for each module. Results were corrected for multiple comparisons after model diagnostics and outlier removal. When significant effects were detected, best linear unbiased predictors (β s or BLUPs) were extracted to estimate the effect at the nodal level and to highlight nodes with the highest contributions (Liu et al., 2008). Nodal Individual Conditional Expectation (ICE) plots were generated to visualize significant effects at the nodal level (Goldstein et al., 2013). These conditional expectation plots were created for each level of the random grouping factor (i.e., for each node) in the interval [-3 3] (this interval was chosen considering the values of the psychometric factors, see Figs. S2b–f). The impact of significant results was investigated also using different graph density thresholds in line with current neuroscientific standards (Nichols et al., 2017; Van den Heuvel et al., 2017).

3. Results

3.1. Questionnaire consistency and factor analysis

Factor analysis yielded five orthogonal factors (factor 1–5). This number of factors (five) was selected as the number of eigenvalues above the 95th percentile from the null distribution generated using parallel analysis (Fig. S2a). Factors showed the highest loadings in the following subscales: factor 1) STAI2, IUS-inhibitory, CAPE-depression, BFI-neuroticism (negative affect); factor 2) SPQ-cognitive perceptual, CAPE-positive, CAPE-negative (psychotic-like experiences); factor 3) IUS-prospective, BFI-extraversion, BFI-agreeableness, BFI-openness (sociality); factor 4) SPQ-interpersonal, SPQ-disorganizational (schizotypal); factor 5) BFI-conscientiousness. The distribution of the factors scores is illustrated in Figs. S2b–f. Participant information, including average, standard deviation, and range for all subscales for both participant groups (full sample, $N = 101$; fMRI sample, $N = 39$) is reported in Table SI. The contribution of each scale to each factor is reported in Table SII. The five factors exhibited normal distributions within the sample (factor 1: $p = .83$; factor 2: $p = .85$; factor 3: $p = .78$; factor 4: $p = .79$; factor 5: $p = .80$; Anderson-Darling test), showing that these factors were acceptable for the implementation in multiple regression models.

Monte Carlo measurements of Tucker's congruence coefficient testing

the robustness of the sample size of the factor analysis suggested a high consistency ($K_{101} \sim 0.95$) as shown in Fig. S2g.

3.2. Identity and agency modulate brain activity in multiple, complementary functional networks

The analysis based on multivariate mixed models yielded thirty-five regions of interest (ROIs) modulated by identity and agency. Increased activity was found in the self-identity (SI) condition (the modulated clusters are visualized in Fig. 2a), compared to the other-identity (OI) condition, in temporal auditory regions ($\alpha < 0.01$, cluster corrected with $p < .001$ and cluster size > 35 voxel) and retroinsular cortex ($\alpha < 0.01$) during the second phase of the trial – which corresponded to the auditory feedback – and in the ventromedial prefrontal cortex ($\alpha < 0.01$) during the first phase of the trial – which corresponded to the word selection process.

The factor agency was associated with activity modulations in many brain areas (the modulated clusters are visualized in Fig. 2b). Regions related to attention and motor processes, like the intraparietal sulcus ($\alpha < 0.001$) and supplementary motor areas ($\alpha < 0.001$), showed higher activity in the self-agency (SA) context throughout the trial. Language-related ventrolateral prefrontal regions ($\alpha < 0.001$), cerebellar regions (left crus I, right crus II, $\alpha < 0.001$), right precuneus ($\alpha < 0.001$), and superior temporal cortex ($\alpha < 0.001$) showed enhanced activity in the SA context during the word selection, but increased activity in the other-agency (OA) context (left inferior frontal gyrus, precuneus) or no modulations (cerebellum) during the auditory feedback. Angular gyrus ($\alpha < 0.001$), left middle frontal gyrus ($\alpha < 0.01$), right superior frontal sulcus ($\alpha < 0.01$), and cerebellar regions (left crus II, right crus I, $\alpha < 0.001$) were deactivated, but stronger deactivations were found in OA trials.

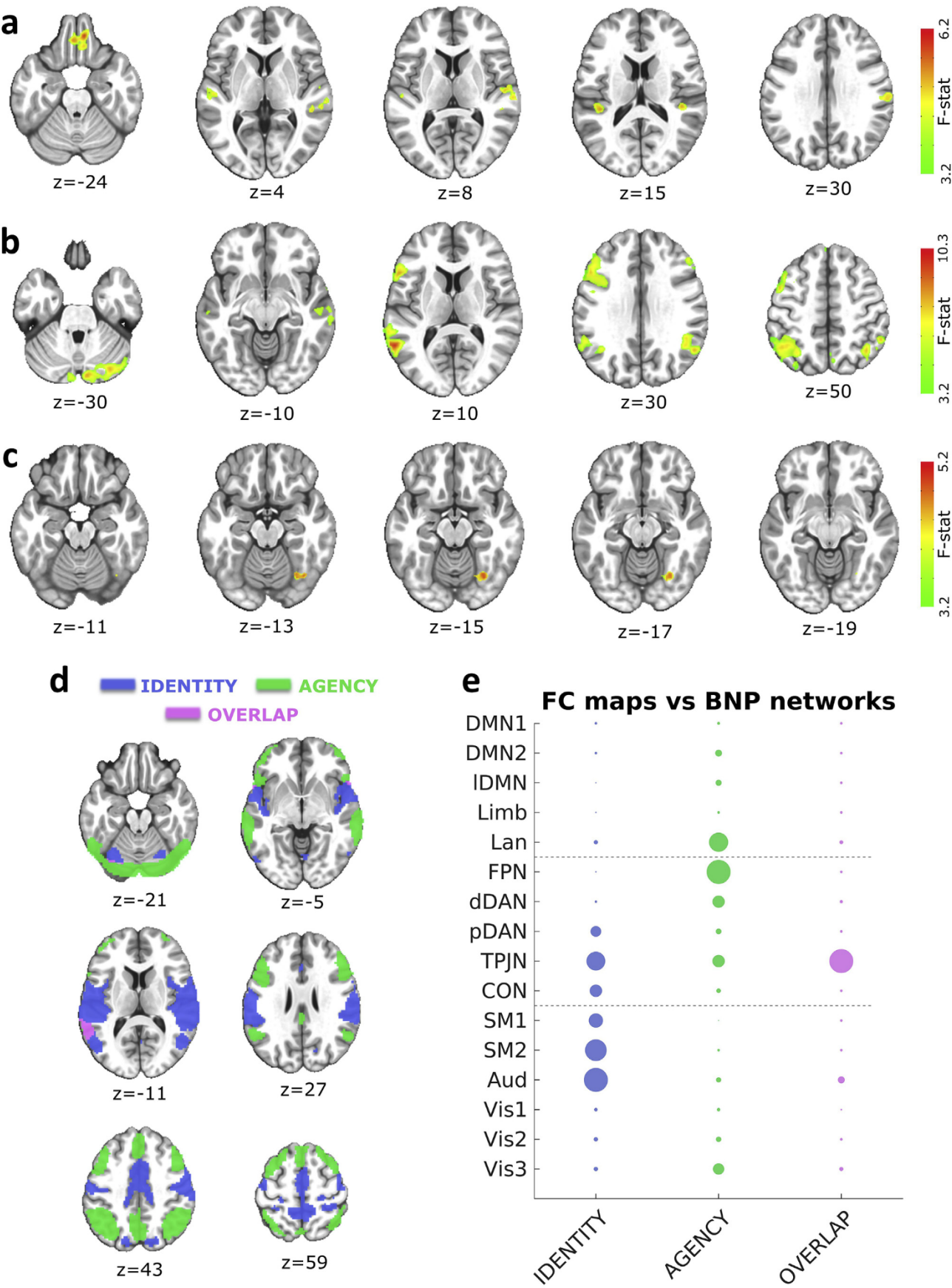
An agency-by-identity interaction was found in the right fusiform gyrus ($\alpha < 0.01$, the modulated cluster is visualized in Fig. 2c), in which the activity was higher in the other-agency condition compared to the self-agency condition during other-identity trials (OI-OA $>$ OI-SA), while the opposite modulation was observed in self-identity trials (SI-OA $<$ SI-SA).

As there may be small volumes with a high significance which are ignored when using a threshold of $p < .001$, Cox recently proposed an equitable thresholding and clustering (ETAC) procedure to simultaneously investigate multiple thresholds (Cox, 2019). To perform an equitable thresholding in our study and to prevent false negatives, we manually investigated multiple thresholds ($p < .005$ & cluster size > 57 ; $p < .001$ & cluster size > 35 ; $p < .0001$ & cluster size > 25). In line with current protocols, we chose to report results associated with $p < .001$ since no additional brain regions nor clusters were found using different thresholds. As reported in the Supplementary File, the results were not affected by the presence of match and no-match trials in the OA condition of the paradigm. The timeline of each ROI is shown in Figs. S3–5.

Seed-based functional connectivity (FC) maps are illustrated in Fig. 2d. The spatial overlap (%) of these FC maps with functional brain networks (Di Plinio and Ebisch, 2018) are reported in Fig. 2e, showing that identity-related ROIs were embedded in sensorimotor, auditory, and cingulo-opercular networks, while agency-related ROIs were associated with executive, language, and attention networks. Notably, the two maps overlapped in the left temporo-parietal junction.

3.3. Psychosis-like experiences and negative affect traits distinctively interact with agency and identity

Three of the psychosis-relevant trait factors (factor 1, negative affect; factor 2, psychosis-like experiences; factor 4, schizotypal traits) showed distinct associations with brain activity in ROIs modulated by identity and agency. Prediction plots were generated to illustrate significant effects during the trial in different conditions. In these charts, the predicted task-evoked activity over time was depicted in relation to different values



(caption on next page)

Fig. 2. Identity and agency modulate brain activity in multiple, complementary functional networks. Results of the multivariate mixed model are displayed (a) for the factor Identity, (b) for the factor Agency, and (c) for their interaction. Results are cluster corrected ($p < .001$, cluster size > 35 voxels; threshold $\alpha < 0.05$). (d) Regions exhibiting strong functional connectivity with ROIs modulated by Identity (blue) and Agency (green) are superimposed on the same MNI standard template. (e) Functional fingerprints of maps presented in (d) with respect to functional networks (Di Plinio and Ebisch, 2018). The correspondence with a brain network was defined as the percentage of the network's voxels that fall within the map, normalized within each map. Particular correspondence is observed for Identity-related ROIs with the auditory network (Aud), with primary (SM1) and secondary (SM2) somatomotor networks, with motor-related control and attentional networks (CON, pDAN), and with the temporo-parietal junction network (TPJN). Agency-related ROIs overlapped mainly with the fronto-parietal control network (FPN), language network (Lan), and dorsal attention network (DAN). The overlap was essentially observed in the temporo-occipito-parietal junction. DMN = Default Mode Network; lDMN = lateral DMN; Limb = Limbic network; Lan = Language network; FPN = Fronto-Parietal Network; dDAN = distal Dorsal Attention Network; pDAN = proximal DAN; TPJN = Temporo-Parietal Junction Network; CON = Cingulo-Opercular control Network; SM1/2 = primary/secondary SensoriMotor network; Aud = Auditory network; Vis1/2-3 = primary/secondary Visual networks.

of the psychometric factor of interest (interval $[-3,3]$). These plots are illustrated in Fig. 3, providing straightforward visualizations of task-specific modulations promoted by the psychometric scores (primary effects of the psychometric factors on brain activity, i.e., without interactions with agency nor identity, are reported in the Supplementary File, Fig. S6).

As shown in Fig. 3a, negative affect traits (psychometric factor 1) were positively related to brain activity in the left retroinsular cortex during SI trials ($t = -3.1$, $p = .002$, $\beta = -0.034$ CI: $[-0.057 \sim -0.012]$, interaction, adjusted model $R^2 = 0.83$), while this effect was absent during OI trials. Thus, the engagement of the retroinsular cortex was enhanced in individuals inclined to experience stress and negative feelings (related to anxiety, depression) when processing auditory stimuli intrinsically related to the self.

ROIs in the bilateral angular gyrus were generally deactivated during task-execution. However, the right inferior angular gyrus showed reduced deactivations with high scores in schizotypal traits (psychometric factor 4), but only in the OA condition ($t = 4.3$, $p = .00002$, $\beta = 0.044$ CI: $[0.024 \sim 0.064]$, interaction, adjusted $R^2 = 0.69$; Fig. 3b). By

contrast, in the bilateral superior angular gyrus, high psychosis-like experience scores (psychometric factor 2) were related to lesser deactivations only in the SA context (left superior angular gyrus: $t = -3.9$, $p = .0001$, $\beta = -0.049$ CI: $[-0.074 \sim -0.024]$, interaction, adjusted $R^2 = 0.74$; right superior angular gyrus: $t = -4.3$, $p = .00002$, $\beta = -0.048$ CI: $[-0.069 \sim -0.026]$, interaction; adjusted $R^2 = 0.68$; Fig. 3c-d). Thus, activity in the superior angular gyrus during SA contexts and activity in the right inferior angular gyrus during OA contexts was enhanced with higher scores in psychosis-like experiences and schizotypal traits, respectively.

3.4. Varying levels of multidimensional self-relatedness reshape the modular organization of the brain

Regarding the graph analyses, two resolution parameters were found to maximize the relative Rand coefficients ($\gamma = 0.9$, $\gamma = 1.7$, Fig. 4a). Fig. 4b illustrates the average FC matrices obtained in the four conditions using $\gamma = 1.7$. Module configurations obtained for $\gamma = 0.9$ are reported in the Supplementary File (Fig. S7). As shown in the figures, six significant

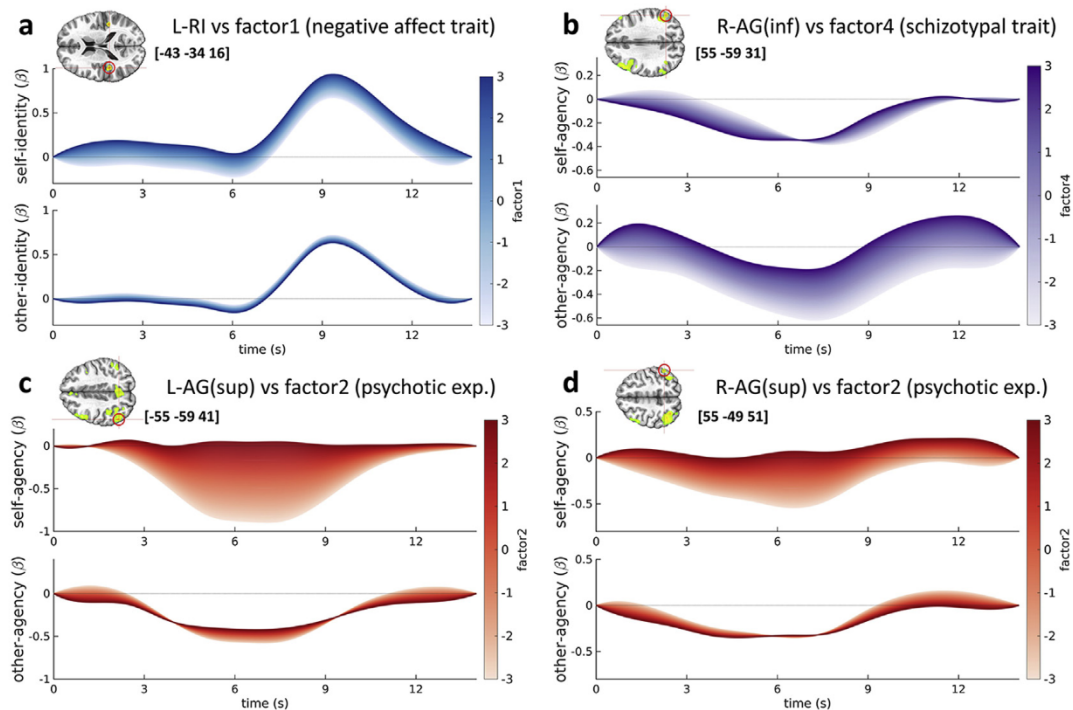


Fig. 3. Psychosis-like experiences and negative affect traits distinctively interact with agency and identity. Each plot illustrates the cubic interpolated predicted activity over time for regions significantly modulated by the interaction factor-by-Identity or factor-by-Agency. MNI coordinates for each significant ROI are also reported.

(a) The left retroinsular cortex (L-RI) showed increased activity with high scores in factor 1 (negative affective trait), but only in the self-identity (SI) condition. (b) The right inferior angular gyrus (R-AGinf) exhibited enhanced activity / suppressed deactivation with high scores in factor 4 (schizotypal traits) in the other-agency (OA) condition. (c,d) The bilateral superior angular gyrus (L-AGsup, R-AGsup) was generally deactivated during the trial, but high scores in factor 2 (psychotic-like experiences) canceled this deactivation in the self-agency (SA) condition.

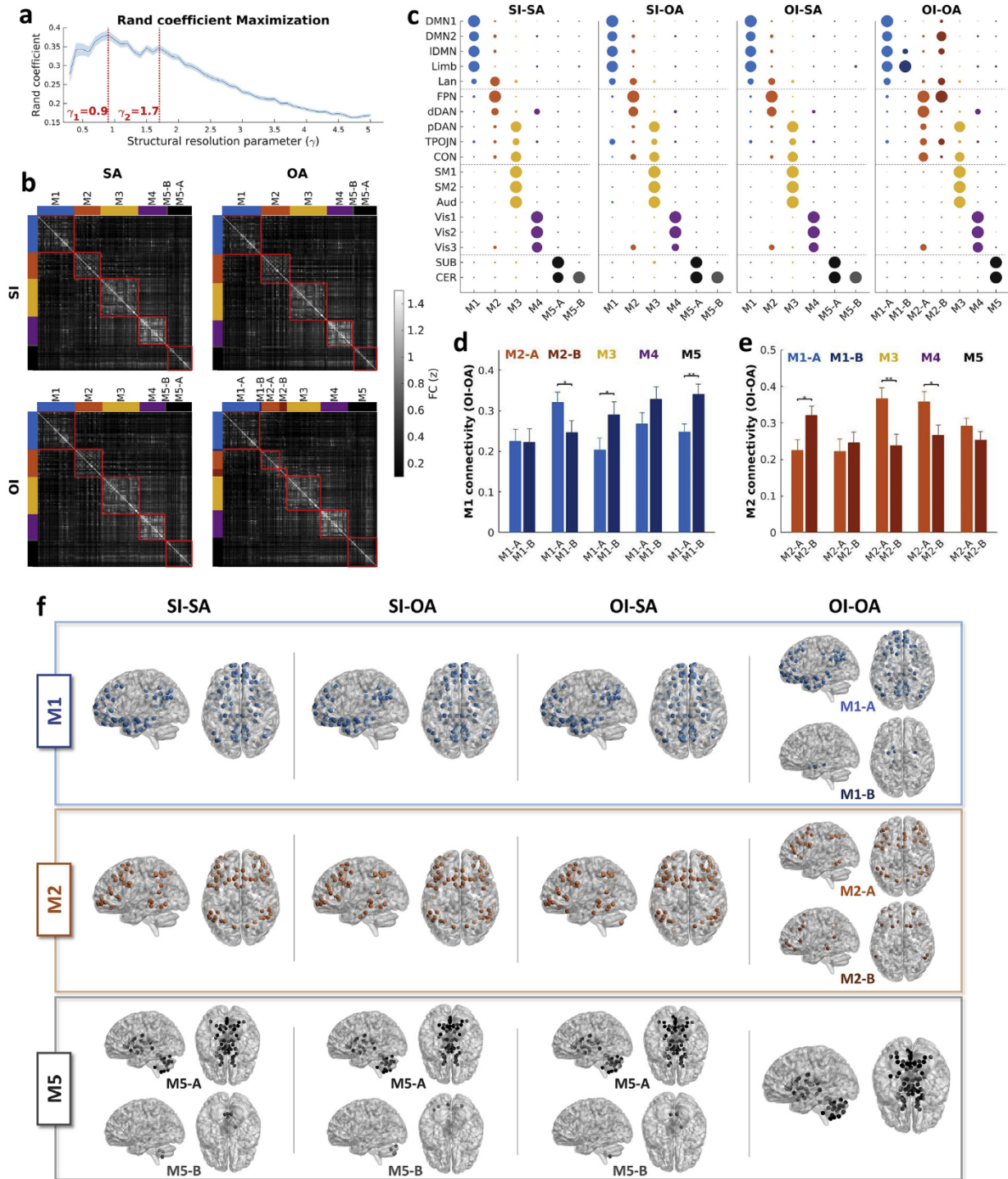


Fig. 4. Varying levels of multidimensional self-relatedness reshape the brain modular organization.

(a) Rand Coefficient maximization. The blue line indicates average scores of the Rand coefficient corresponding to γ values tested in our study (interval [0.3,5.0], 0.1 steps). Shaded lines indicate the standard error. An automated search for local maxima highlighted two peaks among Rand coefficients ($\gamma = 1.7$, $\gamma = 0.9$).

(b) For each experimental condition, the functional connectivity matrix is reported with $\gamma = 1.7$. Each module is enclosed in a red square. Module labels were attributed considering module topographies and pre-existing literature on functional brain networks.

(c) Functional fingerprints of each module ($\gamma = 1.7$) as compared with predefined networks (Di Plinio and Ebisch, 2018). The width of each circle represents the amount of overlap between each network and each module calculated as the percentage of each network covered by each module normalized within each module. SUB = Subcortical nodes; CER = Cerebellar nodes.

(d) Functional profiles of M1-A and M1-B ($\gamma = 1.7$) in the OI-OA condition. The module M1-B was more connected with the sensorimotor module M3 ($p < .01$) and with the cerebellar module M5 ($p < .01$). By contrast, M1-A was more connected than M1-B with M2-B ($p < .05$).

(e) Functional profiles of M2-A and M2-B ($\gamma = 1.7$) in the OI-OA condition. The module M2-A was more connected with the sensorimotor module M3 ($p < .01$) and with the visual module M4 ($p < .05$). By contrast, M2-B was more connected than M2-A with the core default module M1-A ($p < .05$).

(f) Condition-specific modular topographies. Module topographies are reported for each module which showed segregation across experimental conditions. Module labels were attributed considering module topographies and the relationships with pre-existing literature on functional brain networks.

modules were found in the SI-SA, SI-OA, and OI-SA conditions, while seven significant modules were found in the OI-OA condition (threshold: $p < .001$).

Fig. 4c shows the anatomical fingerprints of modules with respect to predefined networks (Di Plinio and Ebisch, 2018). As it can be noted, the topographies of the sensorimotor (M3) and visual (M4) modules were stable across conditions. M3 encompassed both primary and secondary sensorimotor networks (SM1, SM2) as well as cingulo-opercular (CON), proximal dorsal attention (pDAN), auditory (Aud), and temporo-parietal junction (TPJN) networks. The visual module M4 comprised the three visual networks (Vis1, Vis2, Vis3). The two higher-order modules M1 and M2 were related to default and limbic networks (M1: DMN1, DMN2, LDMN, Limb) and to executive/attentional networks (M2: FPN, dDAN), respectively. Both M1 and M2 comprised regions of the language network (Lan).

The modules M1 and M2 (default mode and executive regions, respectively) were segregated in the OI-OA condition. These segregated modules were labeled M1-A/B and M2-A/B for descriptive purposes. Post-hoc comparisons (t-tests) of inter-module FC showed that, in the OI-OA condition, the executive module M2-A (dorsolateral prefrontal cortex, dorsal cingulate, intraparietal sulcus) was more connected with sensorimotor (M3, $p = .003$) and visual (M4, $p = .022$) modules. Instead, the module M2-B (language-related regions and lateral default mode regions) was more connected with the core default mode module M1-A ($p = .015$, Fig. 4d). Moreover, compared to M1-A, the parahippocampal module M1-B was more connected with both sensorimotor (M3, $p = .03$) and subcortical-cerebellar modules (M5, $p = .005$, Fig. 4e). These results indicated that segregated modules in the OI-OA condition showed peculiar connectivity profiles, corroborating the usefulness of the consensus modularity procedure in resolving condition-specific brain modularity.

Finally, subcortical and cerebellar structures exhibited distinctive topologies depending on the condition. While a unified subcortical/cerebellar module (M5) was found in the OI-OA condition, a separate module (M5-B) comprising medial cerebellar structures (lobule IX) were identified in the SA conditions and a separate module encompassing lateral cerebellar regions (crus I-II) was identified in the SI-OA condition.

Modular topographies for M1, M2, and M5 are shown in Fig. 4f. A comprehensive list of regions affiliated to each module is provided in the Supplementary Material.

3.5. Psychosis-like experiences affect cross-networks interactions with incongruent self-relatedness

Two significant effects of psychosis-like experiences (psychometric factor 2) were detected. First, participation coefficients in M3 (sensorimotor module) during the SI-OA condition were negatively associated with factor 2 scores ($t = -2.7$, $p = .007$, $\beta = -0.02$ CI: $[-0.04 \sim -0.01]$, fixed effect, adjusted $R^2 = 0.34$). The extraction of random effect statistics highlighted eight nodes with the largest effects within the module (Fig. 5a–c). These regions were: bilateral superior temporal gyrus (average $t = -2.9$, $p < .01$), bilateral supramarginal gyrus (average $t = -2.5$, $p = .01$), bilateral precentral sulcus (average $t = -3.6$, $p < .001$), and postcentral sulcus ($t = -2.8$, $p = .006$). Second, participation coefficients in M2 (fronto-parietal attentional and executive module) in the OI-SA condition were – again – negatively affected by factor 2 ($t = -2.8$, $p = .005$, $\beta = -0.03$ CI: $[-0.05 \sim -0.01]$, fixed effect, adjusted $R^2 = 0.40$). Fig. 5d–f shows the two nodes in M2 which showed the largest effects, which were located in the right orbitofrontal/fronto-polar cortex (average $t = -3.3$, $p < .001$). Nodal effect sizes (β s) are reported in Fig. 5c and f. Analysis yielded neither significant differences in modularity (p values $> .20$, fixed effects) nor significant associations between modularity and psychological factors (p values $> .10$, fixed effects). Additional results using different graph density thresholds are reported in the Supplementary File (Fig. S8).

In summary, these results show a link between nodal participation

and psychosis-relevant traits in sensorimotor and orbitofrontal/fronto-polar regions with incongruous levels of intrinsic vs extrinsic self-relatedness.

4. Discussion

The self as composed of both intrinsic and extrinsic features parallels the classic dichotomy of William James between the “Me” as the person being known by oneself and the “I” as the subjective knower who intentionally interacts with the environment (James, 1890). The main results of our study in a non-clinical sample showed that these components are naturally unified in a bidirectional process that can be traced to the functional segregation and integration of functional brain networks with relevance for alterations of self-experience.

4.1. Neural activity disentangles the compound structure of the self

Our task-evoked brain activity patterns allowed to dissociate the brain signatures of intrinsic self-features as reflected by voice identity (“This is Me”) from those of extrinsic self-features, like action agency (“I did that”), and also to test their specific relationship with psychosis-relevant traits.

We showed that intrinsic self-relatedness (Northoff, 2011) could be traced to temporal and insular auditory regions that showed stronger activity for self-identity (SI), compared to other-identity conditions (OI), during the perception of the sensory consequences. By contrast, the ventromedial prefrontal cortex, showing stronger activity for SI prior to these consequences, could play an anticipatory role in coding intrinsic self-relatedness of action consequences (Apps and Tsakiris, 2014) through its connections with sensory cortices (Amodio and Frith, 2006). In line with additional contributions of the ventromedial prefrontal cortex to self-monitoring (Northoff and Bermpohl, 2004; Northoff and Panksepp, 2008), our findings suggest that it could play a specific role in prospecting the intrinsic self-relatedness of action outcomes when monitoring self-related sensory consequences.

On the other hand, the processing of extrinsic self-relatedness of action consequences (Haggard, 2005; Gallese and Sinigaglia, 2010) involved regions linked with action performance and planning (i.e., supplementary motor cortex, cerebellum, intraparietal sulcus, premotor cortex). To note, these regions have been consistently associated with the sense of agency in previous studies (Chambon et al., 2013; Moore, 2016; Haggard, 2017; Sperduti et al., 2011). In agreement with the a priori hypothesis, extrinsic self-relatedness also recruited language-related regions (Fu et al., 2005; Chai et al., 2016). The activity in these regions was increased in the self-agency condition (SA) in anticipation of the action consequences and was increased in the other-agency condition (OA) during the subsequent auditory feedback. Notably, the distinction between self- and other-agency was manipulated based on the contextual predictability of the self-relatedness of the action feedback (Haggard, 2017). Hence, this pattern shows that predictions about self-related action consequences arise when coding the sense of agency over intentional actions (Gallese, 2000; Haggard, 2005). It also extends previous reports of suppressed activity when sensory action outcomes match predicted outcomes (Reznik et al., 2014) to higher-order stimuli (words).

In this framework, we report for the first time a differential association of negative affective traits and psychosis-like experiences with the intrinsic and the extrinsic dimension of the self, respectively. On the one hand, the retroinsular cortex responded more strongly during the SI condition in people with increased negative affective traits, suggesting that higher affective traits are linked with stronger self-other identity differentiation. Accordingly, previous studies proposed a role of the posterior insula in the differentiation between self- and other-identity (Heydrich and Blanke, 2013) as well as its dysfunction in schizophrenia (Ebisch et al., 2013). On the other hand, brain activity in the angular gyrus was modulated by the interaction between agency and psychosis-like experiences or schizotypal traits. A role of the angular

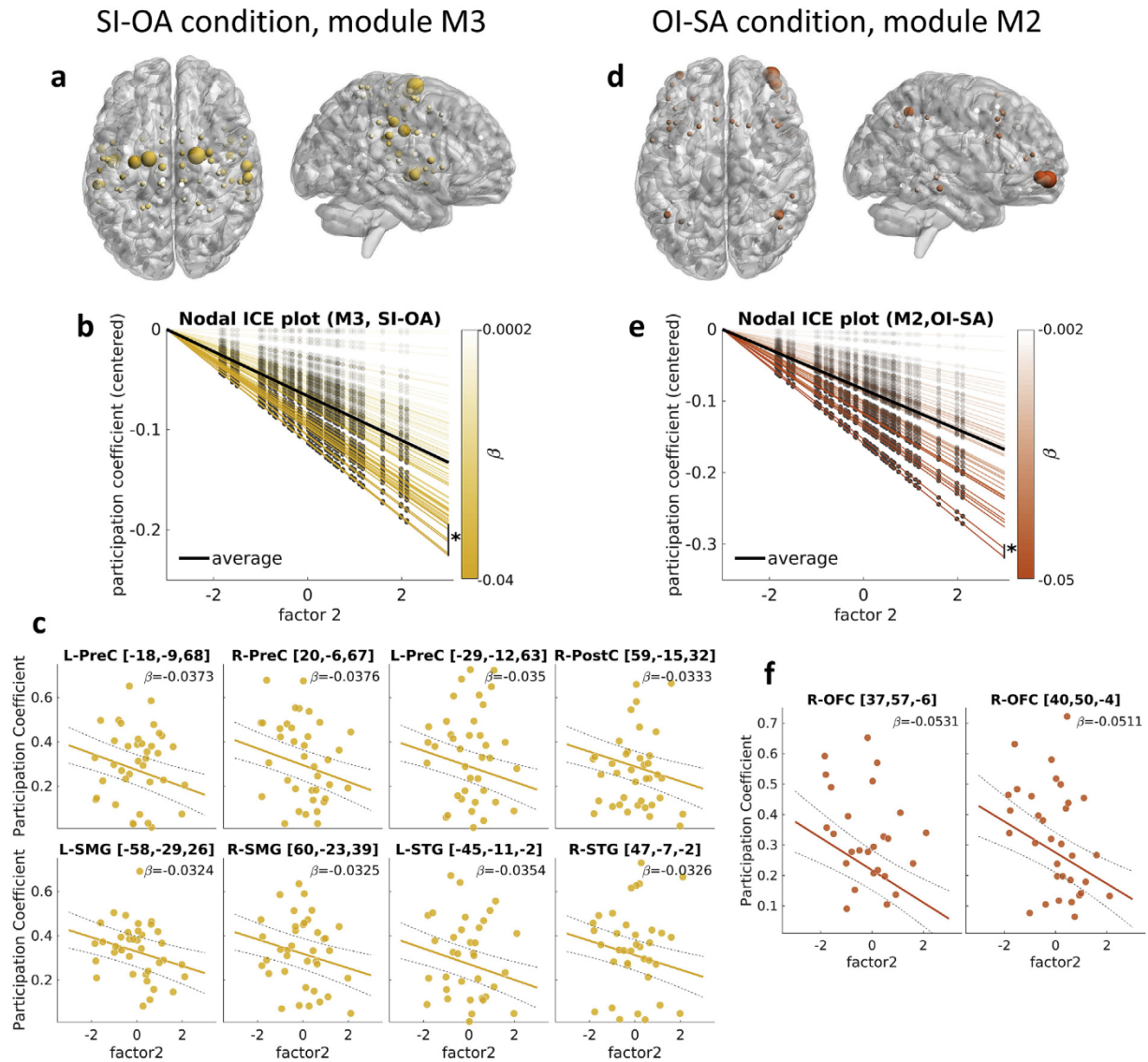


Fig. 5. Psychosis-like experience affects cross-network interactions with incongruent self-relatedness. Figures a-c and d-f illustrate the relationships between factor 2 (psychosis-like experiences trait) and participation coefficients in the SI-OA and OI-SA conditions, respectively.

(a) The size and the color intensity of the nodes in the sensorimotor module M3 indicate the strength of the association between factor 2 and the nodal participation coefficients in the SI-OA condition.

(b) Individual conditional expectation (ICE) plot. Each slope represents predictions of each node within M3. Color intensity indicates the effect strength (β value, estimated using Best Linear Unbiased Predictors, BLUPs).

(c) Nodes of M3 in which the effect of factor 2 was statistically stronger than the average slope. For each node, the p value for the random slope and the center-of-mass coordinates in the MNI space are indicated. Lower participation coefficient means weaker functional connections with the other modules. PreC = Precentral gyrus; PostC = Postcentral gyrus; SMG = Supramarginal gyrus; STG = Superior temporal gyrus.

(d) The size and the color intensity of the nodes in the fronto-parietal module M2 indicate the strength of the association between factor 2 and the nodal participation coefficients in the OI-SA condition.

(e) ICE plot. Each slope represents predictions of each node within M2. Color intensity indicates the effect size (β).

(f) Nodes of M2 in which the effect of factor 2 was statistically stronger than the average slope. OFC = Orbitofrontal cortex.

gyrus has been suggested in the dysfunctional decoding of intentionality and aberrant feedback monitoring in schizophrenia (Backasch et al., 2013; Farrer et al., 2003; Shenton et al., 2010). In particular, this region showed reduced deactivations associated with higher psychosis-related traits. Since regional deactivation is necessary for efficient brain functioning (Leech et al., 2014) and for maintaining optimal performances (Di Plinio et al., 2018), the reduced deactivation in the angular gyrus in people with increased psychosis-like experiences (or schizotypal traits) may indicate a less efficient distinction between self- and other-agency.

These task-evoked activity results illustrate the composite coding of

the intrinsic and extrinsic self-relatedness of external action consequences. In line with our expectations, self-relatedness of verbal auditory action consequences could be decomposed in (i) identity coding in brain regions belonging to sensorimotor, auditory, and cingulo-opercular networks, and (ii) agency processing in attentional, language, and fronto-parietal networks. Mathalon and colleagues (Mathalon et al., 2018) recently showed a reduced suppression of the N1 ERP component when talking as compared to listening to speech in patients with schizophrenia and in individuals with a high clinical risk for psychosis. We expand on these findings by showing that language and auditory networks can

support distinct dimensions of self-relatedness in terms of extrinsic and intrinsic processing, respectively. The complementary nature of these processes could be relevant for explaining psychotic symptoms, as already pointed out by previous studies emphasizing the involvement of aberrant language and auditory processing in verbal auditory hallucinations (Waters and Jardri, 2015). Further developing this clinical potential, we showed in a non-clinical sample that a divergent differentiation between self- and other-agency was related to psychosis-like experiences and schizotypal traits, whereas an increased differentiation between self- and other-identity covaries with negative-affective traits. This picture is consistent with the attribution of psychotic experiences to extrinsic self-disturbances (Nelson et al., 2008; Haggard, 2017), and associations between affective impairments and aberrant intrinsic self-processing (Van der Meer et al., 2010; Hasler and Northoff, 2011) in clinical samples. Future studies are needed to clarify whether these connections of psychometric traits with brain regions related to either extrinsic or intrinsic self-components are also observed for specific symptoms in psychotic disorders.

4.2. Brain network interactions unify extrinsic and intrinsic self-processing

A principal aim of our study was to investigate the self as a multidimensional phenomenon through the analysis of network segregation and integration during the combined processing of intrinsic and extrinsic self-relatedness of external stimuli. Using graph theory, we found that two functional modules were fragmented when self-relatedness was totally missing (i.e., in the other-identity, other-agency condition, OI-OA), while they formed coherent modules when at least one component of the action consequences was self-related. In fact, limbic/memory (i.e., parahippocampal) regions segregated from a core default module (M1-A) to form a distinct module (M1-B) in the OI-OA condition. Furthermore, in the same condition, the module M2 was split in a first module (M2-A) which included fronto-parietal regions related to executive processes (dorsolateral prefrontal cortex, dorsal anterior cingulate cortex) and externally directed actions (intraparietal sulcus, premotor regions) and a second module (M2-B) which included language regions (inferior frontal gyrus, angular gyrus) and secondary default regions (lateral temporal cortex, superior frontal gyrus).

Consistent with previous studies and with our task-evoked activity results, these subsystems were located in default mode (Andrews-Hanna et al., 2014), fronto-parietal control (Dosenbach et al., 2008), and language networks (Chai et al., 2016) that contribute to multidimensional self-processes. Our results suggest a greater functional integration of these brain subsystems when action consequences are self-related, even when only concerning either the extrinsic or the intrinsic self-dimension. Such integrative functioning is probably needed to maintain a coherent sense of the self also in ambiguous contexts. Indeed, discriminating between relevant and irrelevant external stimuli is important in daily life, for instance when identifying one's own speech amidst other voices (Levelt, 1983). One possibility is that the exchange of information across brain systems that contribute to intrinsic and extrinsic self-processing facilitates the integration of the multidimensional self-relatedness of action consequences. Instead, when there is no personal relationship with external stimuli anymore, brain systems involved in self-processing segregate. A similar integrative functioning of brain networks in terms of decreased modularity has been reported in situations of increased conscious awareness of external stimuli (Tononi and Edelman, 1998; Godwin et al., 2015).

Consensus modularity also highlighted context-specific cerebellar modules. Previous studies highlighted a major role of lobules IX/VIIIb in sensorimotor tasks, while crus I-II have been linked with cognitive operations including verb generation and working memory (Stoodley et al., 2009). Besides supporting a role for the cerebellum beyond sensorimotor control (Sokolov et al., 2017), our results suggest a differential arrangement of cerebellar regions depending on the type of sensorimotor interactions with the environment: cerebellar sensorimotor control

(lobule IX) may become more prominent in contexts of higher extrinsic self-relatedness, while cerebellar cognitive engagement (crus I-II) may increase when extrinsic self-incongruence is detected. These results expand the role of the cerebellum in action-feedback monitoring (Van Kemenade et al., 2019), suggesting that distinct cerebellar regions may be involved in the parallel integration of intrinsic and extrinsic self-relatedness of actions.

Finally, we found that individual differences in psychosis-relevant traits in our non-clinical sample were associated with decreases in modular participation with diverging intrinsic and extrinsic self-related information. Two significant effects were identified in individuals with increased psychosis-like experiences (factor 2). When *intrinsic* self-relatedness is lacking (other-identity, self-agency condition, OI-SA), inter-modular connections of regions associated with extrinsic executive control such as the lateral orbitofrontal/frontopolar nodes in the module M2 are restrained. In contrast, when *extrinsic* self-relatedness is absent (self-identity, other-agency condition, SI-OA), sensorimotor regions associated with intrinsic self-relatedness (Gallese and Sinigaglia, 2010; Ebisch and Aleman, 2016), like the precentral gyrus, postcentral gyrus, supramarginal gyrus, and superior temporal gyrus within the module M3 isolate from other modules. This pattern indicates the relevance of the interdependence between intrinsic and extrinsic self-relatedness for psychosis-relevant traits: equivocal self-information in the action feedback in combination with high scores on psychosis-like experiences provokes a loss of “hubness” in specific brain structures. We did not find similar results for default mode, language, and auditory networks. In other words, between-network interactions that support the maintenance of a coherent sense of self in ambiguous contexts could be diminished in individuals with high psychosis-relevant traits through the impairment of cross-network integration in high-level (fronto-parietal) and low-level (sensorimotor) brain networks.

Ambiguous contexts of self-relatedness have already been investigated demonstrating a context-specific effect of psychosis-relevant factors when the agent does not fully control the environment (Moore, 2016; Di Plinio et al., 2019). Moreover, impaired connectivity of intrinsic and extrinsic self-networks has been associated with conditions of auditory-verbal hallucinations characterized by alterations of self-related processing (Ćurčić-Blake et al., 2017). Our results extend these findings, suggesting that the misattribution of action consequences, which is frequent in psychotic conditions, may be related to reduced cross-network interactions of sensorimotor and fronto-parietal executive systems under contexts of ambiguous self-relatedness. Further studies may consider the role of perceived ambiguity in the exacerbation of psychotic symptoms to examine if present results translate to clinical samples. Our findings also deserve to be studied in relation to proposals of meta-monitoring of agency, which were related to schizotypal traits by previous studies (Asai, 2017).

4.3. Conclusion

Our study confirms the hypothesis that the integrative functioning of brain networks supports a multidimensional sense of self. Future studies may consider these findings as a starting point to delineate new experimental paradigms aimed at exploring self-relatedness on multiple dimensions both in healthy and in psychopathological conditions. The brain physiology underlying the sense of self may be further elucidated through a condition-specific evaluation of brain connectomes and of their adaptation to different contexts. Different contents of action feedback and sensory modalities should be taken into account. We argue that a key role of these mechanisms, both behaviorally and neurophysiologically, is to regulate the interactions between the individual and the environment.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neuroimage.2019.116284>.

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